Notice of Allowability	Application No.	Applicant(s)	
	10/018,834	WORRALL, ERIC EDWARD	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the Interview Summary of August 25, 2004*.

2. ☒ The allowed claim(s) is/are *1-10 and 12-49*.

3. ☐ The drawings filed on _____ are accepted by the Examiner.

4. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☒ All b) ☐ Some* c) ☐ None of the:
      1. ☒ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date *8-25-2004* .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

DETAILED ACTION

Status of the Claims

1. In the prior action, mailed December 2, 2003, claims 1-10 and 12-49 were pending and rejected. In the Response filed on June 1, 2004, the Applicant amended claims 13 and 20. Claims 1-10, and 12-49 are currently pending and under consideration.

2. Claims 1-10 and 12-49, as amended in the attached claim set, are allowed.

3. Pages 6-12 represent the amended and allowed claims of the application.

EXAMINER'S AMENDMENT

4. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Bret E. Field on August 25, 2004.

The application has been amended as follows:

The amendment of claim 20, such that the phrase - - a coacervate- - was inserted in the place of the phrase "an absorption complex," was made to clarify that a coacervate of the biologically active molecule and chitosan was required.

The amendments of claims 3, 25, 28, 29, 38, and 39, insert a comma between the last and next-to-last members of the lists in these claims, were made to correct informalities in the form of the claims.

It is also noted that claim 39 was included twice in the listing. One copy of the duplicate claim has been deleted.

Claim Rejections - 35 USC § 112

5. **(Prior Rejection-Withdrawn)** Claims 13-26, and 37-49 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention because it was unclear what was meant by the phrase "at a temperature which finally is in the range of from 40-45° C." In view of the cancellation of the term "finally," the rejection is withdrawn.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. **(Prior Rejections- Withdrawn)** Claims 20-26 were rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over Roser, U.S. Patent 5,149,653 (Roser I), in view of Illum et al. (U.S. Patent 6,391,318) and Chatfield (U.S. Patent 6,136,606), and in view of Roser et al., WO 96/40077 (Roser PCT), and Roser et al, U.S. Patent 6,221,575 (Roser II). The

Applicant has amended the rejected claims to require that the claimed compositions form an "absorption complex" of the desiccated biological material and chitosan. Claims 1-3, 5-10, 12-14, 16-25, 27-29, 31, 33-39, 41-43, 45-49 were rejected under 35 U.S.C. 103(a) as being unpatentable over Roser, U.S. Patent 5,149,653 (Roser I), in view of Illum et al. (U.S. Patent 6,391,318) and Chatfield (U.S. Patent 6,136,606), and in view of Roser et al., WO 96/40077 (Roser PCT), and Roser et al, U.S. Patent 6,221,575 (Roser II), and further in light of the teachings of Herbert et al (U.S. Patent 5,654,008) and Orly et al. (US Patent 5,672,301). Claim 4 was rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over Roser I, in view of Illum, Chatfield, Roser PCT, and Roser II as applied to claims 1-3, 5, 6, 20, and 22 above, and further in view of Rweyemamu et al., Revue Scientifique et technologique 14(3), 593-601 and Gombotz et al., U.S. Patent 5,900,238. Claims 1, 2, 5, 7-10, 2-14, 16-24, 27, 28, 31, 33-38, 41-43, and 45-48, were rejected under 35 U.S.C. 103(a) as being unpatentable over Roser, U.S. Patent 5,149,653 (Roser I), and in view of Roser et al., WO 96/40077 (Roser PCT), and Roser et al, U.S. Patent 6,221,575 (Roser II), and further in view of the teachings of Roy et al., U.S. Patent 5,972,707.

The Applicant traverses these rejections on the grounds that none of these references suggests the use of a trehalose with coacervate of chitosan with a biologically active molecule in order to preserve the molecule. The arguments are found persuasive. The rejections are therefore withdrawn.

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

James C. Housel 9/7/04

JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

1. (Previously Presented) A method of preserving biologically-active material comprising mixing an aqueous suspension of the biologically-active material with a sterile aqueous solution of chitosan or a non-toxic salt thereof to form a coacervate of the biologically-active material and chitosan or non-toxic salt thereof, adding to the coacervate a sterile aqueous solution of trehalose, subjecting the sterile mixture of coacervate and trehalose to drying at a pressure less than atmospheric and at a temperature which is initially less than or equal to 37°C and thereafter may fall provided that the temperature does not fall to, or below, 0°C to form a glassy porous matrix comprising metastable glassy trehalose containing, within the matrix, desiccated biologically-active material and chitosan or non-toxic salt thereof.

2. (Original) A method according to claim 1, wherein the biologically-active material is selected from viruses, bacteria, tertiary structured biologically-active protein and nucleic acid.

3. (Currently Amended) A method according to claim 2, wherein the biologically-active material is at least one virus selected from Rinderpest Virus, Peste de Petit Ruminants Virus, Measles, Mumps, Rubella, Yellow Fever, Polio, and Newcastle Disease Virus.

4. (Previously Presented) A method according to claim 2, wherein the biologically-active material is *Mycoplasma mycoides*.

5. (Original) A method according to any one of claims 1 to 4, wherein the sterile aqueous solution of chitosan or non-toxic salt thereof has a chitosan concentration of 0.01% w/v.

6. (Original) A method according to claim 5, wherein the sterile aqueous chitosan solution and the aqueous suspension of biologically-active material are mixed at a volume ratio of 1:1 at pH 7.4.

7. (Previously Presented) A method according to claim 1, wherein the coacervate of biologically-active material and chitosan is subjected to vortex mixing.

8. (Previously Presented) A method according to claim 1, wherein the coacervate of biologically-active material and chitosan is mixed with a sterile aqueous trehalose solution having a trehalose concentration in the range of from 0.20 to 20% w/v.

9. (Original) A method according to claim 8, wherein the sterile aqueous solution of trehalose has a trehalose concentration in the range of from 2.5 to 8% w/v.

10. (Original) A method according to claim 9, wherein the sterile aqueous solution of trehalose has a trehalose concentration of about 5% w/v.

11. (Canceled)

12. (Previously Presented) A method according to claim 1, wherein the drying stage is carried out at a pressure of not greater than 800 mbar.

13. (Previously Presented) A method according to claim 1, wherein the resulting trehalose matrix containing desiccated biologically-active material and chitosan or non-toxic salt thereof is subjected to a secondary drying procedure for 10 to 30 hours at a pressure not greater than 0.1 mbar and at a temperature which is in the range of from 40 to 45°C to form a trehalose matrix having a residual moisture content of not greater than

2% containing, within the matrix, desiccated biologically-active material and chitosan or non-toxic salt thereof.

14. (Previously Presented) A method according to claim 13, wherein secondary drying is carried out for 20 to 30 hours.

15. (Original) A method according to claim 13, wherein secondary drying is carried out for 15 to 17 hours at a temperature of about 37°C and the temperature is, thereafter, raised gradually over the remaining secondary drying time to a final temperature in the range of from 40 to 45°C.

16. (Previously Presented) A method according to claim 13, wherein the residual moisture content at the end of the secondary drying step is 1.0% or lower.

17. (Previously Presented) A method of making a vaccine comprising preserving a biologically-active material according to the method of claim 1 and rehydrating the glassy product obtained thereby in an appropriate aqueous medium.

18. (Previously Presented) A method according to claim 17, wherein the vaccine is for oral or intranasal use.

19. (Original) A method according to claim 17, wherein the vaccine is a Measles, Mumps, Rubella (MMR) vaccine.

20. (Currently Amended) A rehydratable composition comprising trehalose in the form of a metastable glass matrix containing, within the matrix, ~~an absorption complex~~ **a coacervate** of a desiccated biologically-active material and chitosan or a non-toxic salt thereof.

21. (Previously Presented) A rehydratable composition according to claim 20 which has a residual moisture content of not greater than 2%.

22. (Previously Presented) A rehydratable composition according to claim 21 which has a residual moisture content of not greater than 1%.

23. (Previously Presented) A rehydratable composition according to claim 20, useful on rehydration for making a vaccine.

24. (Previously Presented) A rehydratable composition according to claim 20, wherein the biologically-active material is selected from viruses, bacteria, tertiary structured biologically-active proteins and nucleic acids.

25. (Currently Amended) A rehydratable composition according to claim 24, wherein the biologically-active material is at least one virus selected from Rinderpest Virus, Peste de Petit Ruminants Virus, Measles, Mumps, Rubella, Yellow Fever, Polio**,** **Myelitis** ~~-~~and Newcastle Disease Virus.

26. (Previously Presented) A rehydratable composition according to claim 24, wherein the biologically-active material is *Mycoplasma mycoides*.

27. (Previously Presented) A method of preserving biologically-active material comprising mixing an aqueous suspension of the biologically-active material with a sterile aqueous solution of chitosan or a non-toxic salt thereof to form a coacervate of the biologically-active material and chitosan or non-toxic salt thereof, adding to the coacervate a sterile aqueous solution of trehalose, subjecting the sterile mixture of coacervate and trehalose to drying for a period of 30 to 60 minutes at a pressure less than atmospheric and at a temperature, which is initially less than or equal to 37°C and thereafter may fall provided that the temperature does not fall to, or below 0°C and wherein the final temperature is less than or equal to

40°C to form a glassy porous matrix comprising metastable glassy trehalose having a residual moisture content of less than or equal to 10% containing, within the matrix, desiccated biologically-active material and chitosan or non-toxic salt thereof.

28. (Currently Amended) A method according to claim 27, wherein the biologically-active material is selected from viruses, bacteria, tertiary structured biologically-active protein, and nucleic acid.

29. (Currently Amended) A method according to claim 28, wherein the biologically-active material is at least one virus selected from Rinderpest Virus, Peste de Petit Ruminants Virus, Measles, Mumps, Rubella, Yellow Fever, Polio, and Newcastle Disease Virus.

30. (Previously Presented) A method according to claim 28, wherein the biologically-active material is *Mycoplasma mycoides*.

31. (Previously Presented) A method according to claim 27, wherein the sterile aqueous solution of chitosan or non-toxic salt thereof has a chitosan concentration of 0.01% w/v.

32. (Previously Presented) A method according to claim 31, wherein the sterile aqueous chitosan solution and the aqueous suspension of biologically-active material are mixed at a volume ratio of 1:1 at pH 7.4.

33. (Previously Presented) A method according to claim 27, wherein the coacervate of biologically-active material and chitosan is subjected to vortex mixing.

34. (Previously Presented) A method according to claim 27, wherein the coacervate of biologically-active material and chitosan is mixed with a

sterile aqueous trehalose solution having a trehalose concentration in the range of from 0.20 to 20% w/v.

35. (Previously Presented) A method according to claim 34, wherein the sterile aqueous solution of trehalose has a trehalose concentration in the range of from 2.5 to 8% w/v.

36. (Previously Presented) A method according to claim 27, wherein the drying stage is carried out at a pressure of not greater than 800 mbar.

37. (Previously Presented) A method of preserving biologically-active material comprising mixing an aqueous suspension of the biologically-active material with a sterile aqueous solution of chitosan or a non-toxic salt thereof to form a coacervate of the biologically-active material and chitosan or non-toxic salt thereof, adding to the coacervate a sterile aqueous solution of trehalose, subjecting the sterile mixture of coacervate and trehalose to drying for a period of from 30 to 60 minutes at a pressure not greater than 800 mbar and at a temperature which is initially less than or equal to 37°C and thereafter may fall provided that the temperature does not fall to, or below, 0°C to form a glassy porous matrix comprising metastable glassy trehalose having a residual moisture content of less than or equal to 10% containing, within the matrix, desiccated biologically-active material and chitosan or non-toxic salt thereof, and then subjecting the resulting trehalose matrix containing desiccated biologically-active material and chitosan or non-toxic salt thereof to a secondary drying procedure for 10 to 30 hours at a pressure not greater than 0.1 mbar and at a temperature which is in the range of from 40 to 45°C to form a trehalose matrix having a residual moisture content of not greater than 2% containing, within the matrix, desiccated biologically-active material and chitosan or non-toxic salt thereof.

38. (Currently Amended) A method according to claim 37, wherein the biologically-active material is selected from viruses, bacteria, tertiary structured biologically-active protein, and nucleic acid.

39. (Currently Amended) A method according to claim 38, wherein the biologically-active material is at least one virus selected from Rinderpest Virus, Peste de Petit Ruminants Virus, Measles, Mumps, Rubella, Yellow Fever, Polio, and Newcastle Disease Virus.

~~39. (Previously Presented) A method according to claim 38, wherein the biologically-active material is at least one virus selected from Rinderpest Virus, Peste de Petit Ruminants Virus, Measles, Mumps, Rubella, Yellow Fever, Polio and Newcastle Disease Virus.~~

40. (Previously Presented) A method according to claim 38, wherein the biologically-active material is *Mycoplasma mycoides*.

41. (Previously Presented) A method according to claim 37, wherein the coacervate of biologically-active material and chitosan is mixed with a sterile aqueous trehalose solution having a trehalose concentration in the range of from 0.20 to 20% w/v.

42. (Previously Presented) A method according to claim 41, wherein the sterile aqueous solution of trehalose has a trehalose concentration in the range of from 2.5 to 8% w/v.

43. (Previously Presented) A method according to claim 37, wherein secondary drying is carried out for 20 to 30 hours.

44. (Previously Presented) A method according to claim 37, wherein secondary drying is carried out for 15 to 17 hours at a temperature of

about 37°C and the temperature is, thereafter, raised gradually over the remaining secondary drying time to a final temperature in the range of from 40 to 45°C.

45. (Previously Presented) A method according to claim 37, wherein the residual moisture content at the end of the secondary drying step is 1.0% or lower.

46. (Previously Presented) A method of making a vaccine comprising preserving a biologically-active material according to the method of claim 27 and rehydrating the glassy product obtained thereby in an appropriate aqueous medium.

47. (Previously Presented) A method of making a vaccine comprising preserving a biologically-active material according to the method of claim 37 and rehydrating the glassy product obtained thereby in an appropriate aqueous medium.

48. (Previously Presented) A method according to claim 47, wherein the vaccine is for oral or intranasal use.

49. (Previously Presented) A method according to claim 47, wherein the vaccine is a Measles, Mumps, Rubella (MMR) vaccine.